

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY  
(CHAPTER I OR CHAPTER II  
OF THE PATENT COOPERATION TREATY)  
(PCT Rules 44bis.3(c) and 72.2)

To:

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Date of mailing ( <i>day/month/year</i> ) 29 June 2006 (29.06.2006)	
Applicant's or agent's file reference PH-2267-PCT	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/JP2004/014452	International filing date ( <i>day/month/year</i> ) 24 September 2004 (24.09.2004)
Applicant KYOWA HAKKO KOGYO CO., LTD. et al	

**1. Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

**2. Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

**3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Masashi Honda
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 70 10

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference PH-2267-PCT	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/JP2004/014452	International filing date ( <i>day/month/year</i> ) 24 September 2004 (24.09.2004)	Priority date ( <i>day/month/year</i> ) 24 September 2003 (24.09.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant KYOWA HAKKO KOGYO CO., LTD.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	Date of issuance of this report 20 June 2006 (20.06.2006)  Authorized officer <p style="text-align: center; font-weight: bold;">Masashi Honda</p> Telephone No. +41 22 338 70 10
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# PATENT COOPERATION TREATY

TRANSLATION

From the  
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:		
		Date of mailing (day/month/year)
Applicant's or agent's file reference <b>PH-2267-PCT</b>		<b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. <b>PCT/JP2004/014452</b>	International filing date (day/month/year) <b>24.09.2004</b>	Priority date (day/month/year) <b>24.09.2003</b>
International Patent Classification (IPC) or both national classification and IPC		
Applicant <b>KYOWA HAKKO KOGYO CO., LTD.</b>		

1. This opinion contains indications relating to the following items: <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 5%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 25%;">Box No. I</td> <td>Basis of the opinion</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the opinion	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VII	Certain defects in the international application																							
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
2. <b>FURTHER ACTION</b> If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220.																									
3. For further details, see notes to Form PCT/ISA/220.																									

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/014452

Box No. 1

Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☒ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☒ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2004/014452

Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 12-15

because:

☒ the said international application, or the said claims Nos. 12-15  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 12-15 relate to a method for surgery or treatment of the human body.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported  
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 12-15

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/JP2004/014452

**Box No. V** Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

**1. Statement**

Novelty (N)	Claims	1-11	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-11	NO
Industrial applicability (IA)	Claims	1-11	YES
	Claims		NO

**2. Citations and explanations:**

**Documents**

Document 1: Cancer Research, 1998, Vol. 58, No. 15, pages 3353-3361  
 Document 2: Current Cancer Drug Targets, 2002, Vol. 2, No. 3, pages 191-207  
 Document 3: JP, 2002-512792, A (Genesense Technologies Inc.), 8 May, 2002 (08.05.2002)  
 Document 4: JP, 09-501411, A (Bicher, Haim, I.), 10 February, 1997 (10.02.97)  
 Document 5: JP, 2003-520195, A (Imclone Systems Inc.), 2 July, 2003 (02.07.03)

**Description**

**Claims 1-11**

The subject matters of claims 1-11 appear to be novel since they are not disclosed in any of the documents cited in the ISR, but do not appear to involve an inventive step in view of documents 1-5 cited in the ISR.

Documents 1 and 2 describe that effect can be obtained by inhibiting an IGF-I receptor with methods like dominant negative body expression of an IGF-I receptor or medication of an anti-senses RNA so as to obtain anti-cancer effect such as controlling of cancer metastasis, canceration and vascularization. Moreover, document 1 describes that IGF-I, a ligand of IGF-I receptor, and IGF-II are both capable of activating adhesion that is the first step and cellular infiltration that is an important step of metastasis cascade and preventing cancer metastasis and recurrence by targeting IGF-I. For activating and preventing, document 1 describes that there are a method targeting an IGF-I receptor and a method targeting both of IGF-I, a ligand of the IGF-I receptor, and IGF-II. Document 2 describes that an IGF-I/IGF-I receptor system promotes cancer metastasis, and IGF-I adjusts expression of matrix metaprotease-2 which takes a central part of cancer intrusion and metastasis. Furthermore, document 3 describes that IGF-II contributes proliferation and metastasis of various cancers, and also describes that metastasis can be controlled by giving IGF-II anti-sense oligonucleotide in order to inhibit IGF-II.

In addition, as described in documents 4 and 5, it is usually performed to use various kinds of treatment such as chemical therapy with anti-cancer drugs and radiation exposure therapy at the same time in cancer treatment.

Therefore, a person skilled in the art could have easily conceived of inhibiting activation of both of IGF-I and IGF-II, which contribute proliferation and metastasis of cancer, by using publicly known methods such as an antibody and of applying other anti-cancer drugs or radiation exposure therapy at the same time.